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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,520	11/16/2005	Hideji Tajima	4986-0103PUS1	9089

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EXAMINER	
BOWERS, NATHAN ANDREW	
ART UNIT	PAPER NUMBER
1775	

NOTIFICATION DATE	DELIVERY MODE
02/02/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/531,520	TAJIMA ET AL.	
	Examiner	Art Unit	
	NATHAN A. BOWERS	1775	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8,10-18,31-36 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8,10-18,31-36 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 18 November 2010 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1, 4-8, and 31-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan (US 5753477) and Eddelman (US 3985649) as applied to claim 1, and further in view of Dzekunov (US 20030073238).

With respect to claim 1, Chan discloses an apparatus for introducing a biological material which has one or more packing units capable of accommodating a plurality of cells and a mixture solution containing magnetic supports carrying a biological material. This is disclosed in column 5, line 42 to column 6, line 59. Column 4, lines 32-62 state that an introduction treatment unit is used to control a magnetic force affecting the inside of the packing unit from at least two directions so as to move the magnetic supports relative to the host cells in order to introduce the supports and biological material into the host cells. Chan, however, does not expressly state that the magnets of the introduction treatment unit are vertically translatable so as to move magnetic supports grouped in a planar form along a direction normal to a developed surface of the planar form.

Eddelman discloses a system for mixing and separating biological materials using magnetic supports (Figure 7:33) within a reaction chamber/packing unit (Figure 7:31). A magnet (Figure 7:30) is provided adjacent to reaction chamber, and is capable of grouping the magnetic supports to create a planar form (Figure 9:37) within the reaction chamber. As depicted in Figures 7 and 8, the magnet is moved in an up and down motion in order to move magnetic supports grouped in a planar form along a direction normal to a developed surface of the planar form. This is disclosed in column 5, lines 41-53.

Chan and Eddelman are analogous art because they are from the same field of endeavor regarding magnetic mixing and separation systems.

At the time of the invention, it would have been obvious to ensure that the magnets disclosed by Chan were capable of being moved up and down along the vertical walls of the packing units. One of ordinary skill would have recognized that this would have allowed the magnetic particles to contact and transfect a greater percentage of cells within the packing unit. Vertical movement of the Chan magnetic particles across the length of the packing unit during treatment would have enhanced the introduction of biological materials through the engagement of cells located at every fluidic level.

Chan and Eddelman, however, still differ from Applicant's claimed invention. Chan discloses that a magnetic source is used to apply a magnetic field capable of moving the magnetic supports relative to the host cells. Chan, however, does not

expressly state that the magnetic source is controlled using a control unit, or that a pressure adjuster is used to draw and discharge solution within the packing unit.

Dzekunov discloses a flow cell adapted for the transfection of biological cells with foreign matter. A flow channel (Figure 13:40) is provided in communication with electrode plates (Figure 13:10) configured to create an electrical field capable of porating a cell. This is described in paragraph [0249]. Paragraphs [0199] and [0200] indicate that the operation of the system is regulated using a control unit. Dzekunov additionally teaches that cells are porated within a liquid passage (Figure 13:40), and that the fluid flow through the passage is regulated using a plurality of valves and pumping means. The valves and pumping means of Dzekunov serve as pressure adjusters because they are used to increase and decrease the fluid pressure within the passage at any given time.

Chan and Dzekunov are analogous art because they are from the same field of endeavor regarding the introduction of biomolecules into biological cells.

At the time of the invention, it would have been obvious to ensure that the magnets of Chan are operated using a control unit. As evidenced by Dzekunov, automatic controllers are considered to be well known in the art, and useful for the regulation of a complex system. One of ordinary skill would have recognized that control units are efficient, cost effective and capable of operating a particular unit (such as a magnet) with a high degree of precision and accuracy.

At the time of the invention, it also would have been obvious to construct the Chan apparatus as a flow chamber system comprising a liquid passage suited for

communication with the introduction treatment unit. Dzekunov teaches it is desirable to provide a flow cell with valves and pumps capable of regulating and correcting the pressure during experimentation. One of ordinary skill in the art would have understood that the apparatus of Chan naturally calls for accumulating cells and magnetic particles within a packing unit formed as a liquid passage, modifying the cells by applying a magnetic force, and then removing the modified cells from the flow chamber through the operation of valves and pumps.

With respect to claim 4, Chan, Eddelman and Dzekunov disclose the apparatus in claim 1. Chan additionally teaches that the magnetic supports have a major axis and a size allowing entry into the host cells. Column 5, lines 1-40 indicate that the supports are ideally situated for cell penetration.

With respect to claim 5, Chan, Eddelman and Dzekunov disclose the apparatus in claim 1. Furthermore, Chan indicates that an introduction adjuvant for helping to introduce the biological material is provided. In column 5, lines 33-40, Chan indicates that the magnetic supports are coated with a biologically inert material in order to improve and facilitate transfection.

With respect to claim 6 and 7, Chan, Eddelman and Dzekunov disclose the apparatus in claims 4 and 5, wherein the apparatus is fully capable of manipulating magnetic supports of essentially any shape compatible with cell penetration. The

packing unit and introduction treatment unit of Chan are fully capable of interacting with a wide variety of magnetic supports.

With respect to claim 8, Chan, Eddelman and Dzekunov disclose the apparatus in claim 1 wherein the introduction treatment unit performs introduction treatment based on the properties, amount and density of the host, biological material and magnetic supports.

With respect to claims 31-36, Chan, Eddelman and Dzekunov disclose the combination as previously described above. Chan describes packing units capable of accommodating a plurality of cells and a mixture solution containing magnetic supports carrying a biological material. This is disclosed in column 5, line 42 to column 6, line 59. Column 4, lines 32-62 state that an introduction treatment unit is used to control a magnetic force affecting the inside of the packing unit from at least two directions so as to move the magnetic supports relative to the host cells in order to introduce the supports and biological material into the host cells. Additionally, Eddelman discloses that it is known in the art to selectively move external magnets in order to affect the motion of magnetic particles within a reaction chamber. Chan, however, does not expressly state that a perforation treatment unit is provided.

Dzekunov discloses a flow cell adapted for the transfection of biological cells with foreign matter. A flow channel (Figure 13:40) is provided in communication with electrode plates (Figure 13:10) configured to create an electrical field capable of

porating a cell. This is described in paragraph [0249]. The electrode system is considered to be a perforation treatment unit because it is used to electroporate cell membranes.

At the time of the invention, it would have been obvious to provide the Chan system with an electroporation system similar to that set forth by Dzekunov. Dzekunov teaches that electroporation is a useful technique that allows one to reversibly porate a plurality of biological cells in solution without permanently damaging the cell membrane. One of ordinary skill would have found it beneficial to first porate the host cells in Chan through the creation of an electric field before puncturing them with the magnetic supports. This would have reduced the trauma experienced by the cells and would have improved transfection frequency.

2) Claims 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan (US 5753477), Eddelman (US 3985649) and Dzekunov (US 20030073238) as applied to claim 1, and further in view of Lafferty (US 20030096220).

With respect to claims 10-12, Chan, Eddelman and Dzekunov disclose the apparatus set forth in claim 1, however do not expressly indicate that a plurality electromagnets are provided in communication with a transfer element for movement around the packing unit.

Lafferty discloses a capillary device for screening biological analytes comprising a plurality of magnets capable of interacting with magnetic beads within the capillary. Lafferty teaches in paragraph [0380] that a plurality of magnet blocks are provided in

communication with the capillary, and are capable of being mechanically being moved up and down the capillary using a plurality of holders. This is depicted in Figure 7B.

Chan and Lafferty are analogous art because they are from the same field of endeavor regarding the manipulation of magnetic particles in microfluidic biological testing devices.

At the time of the invention, it would have been obvious to provide the Chan system with a plurality of magnet blocks capable of being moved relative to the packing unit. Lafferty teaches that varying the distance and location of magnetic blocks in relation to suspended magnetic particles in a solution allows one to better affect the motion of the magnetic particles. The use of a plurality of magnetic blocks operated by mechanical holders would have allowed given one an enhanced ability to manipulate the magnetic supports of Chan so as to better effectuate transfection. The addition of multiple magnetic blocks and corresponding holders to the Chan system would be completed in a predictable manner and would yield predictable results.

With respect to claim 13, Chan, Eddelman and Dzekunov disclose the apparatus set forth in claim 1, however do not expressly indicate that the magnet source is an annular magnet source capable of movement along the packing unit. As noted above, Lafferty discloses a plurality of mechanical moving means capable of transporting magnet blocks across the length of a capillary tube in order to affect magnetic supports within the tubes. Although Chan and Lafferty each fail to disclose the use of annular magnets, one of ordinary skill would have understood to form the magnets of Chan

according to any known shape capable of providing attractive and repulsive forces to the supports in solution. The use of an annular magnet is functionally equivalent to the use of magnets formed as other shapes, and therefore the use of an annular magnet is not patentably distinguishable over the prior art. See MPEP 2144.04.

With respect to claims 14-16, Chan, Eddelman and Dzekunov disclose the apparatus set forth in claim 1, however do not expressly disclose the use of a plurality of packing units arranged along a horizontal line, and a plurality of magnetic sources configured to interact with the plurality of packing units. As set forth above, Lafferty discloses a plurality of capillary tubes (see Figure 7B) arranged in parallel, and a plurality of magnet blocks each capable of communicating with a respective tube and moving across the length of a respective tube.

At the time of the invention, it would have been obvious to one of ordinary skill in the art to operate a plurality of the Chan packing tubes in parallel so that each packing unit is operated simultaneously by a respective magnet block. One of ordinary skill would have understood that this arrangement would have been beneficial because it would have served to increase throughput and improve efficiency.

3) Claims 17, 18 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan (US 5753477), Eddelman (US 3985649) and Dzekunov (US 20030073238) as applied to claim 1, and further in view of Blankenstein (US 20030044832).

Chan, Eddelman and Dzekunov disclose the apparatus set forth in claim 1, however do not expressly indicate that a magnetic separation unit is provided for isolating magnetic particles.

Blankenstein discloses a magnetic separation unit comprising a packing unit through which magnetic supports (Figure 1:12) and non-magnetic particles (Figure 1:13) are allowed to flow. A magnet (Figure 1:8) is provided for separating the magnetic supports from the remainder of the mixture solution by causing the magnetic supports to deviate toward a different fluid outlet (Figure 1:6). This is disclosed in paragraph [0132].

Chan and Blankenstein are analogous art because they are from the same field of endeavor regarding magnetic manipulation of biological particles.

At the time of the invention, it would have been obvious to provide the packing unit of Chan with a magnetic separation unit capable of recovering and isolating host cells transfected with a magnetic support. Blankenstein is evidence that one of ordinary skill would have been able to use a magnetic separation unit in the system of Chan in order to efficiently and accurately separate transfected cells for undesirable components within the fluid mixture. One of ordinary skill would have found this to be a desirable way to quickly isolate the magnetic supports for further downstream processing.

Response to Amendment

It is noted that the claims filed 18 November 2010 do not include a listing of all claims (i.e. do not include cancelled claims under the claim identifier of "cancelled").

See MPEP 714. Because this is a minor informality, a notice of non-compliant amendment has not been issued in order to expedite prosecution.

Response to Arguments

In response to Applicant's amendments filed 18 November 2010, the rejections under 35 U.S.C. 112 have been withdrawn.

Applicant's arguments filed 18 November 2010 with respect to the 35 U.S.C. 103 rejections involving the combination of Chan, Eddelman and Dzekunov have been fully considered but they are not persuasive.

Applicant's principle arguments are

(a) Eddelman is not prior art because Eddelman relates to the extraction of a target substance from a cell or bacteria.

In response, please consider the following remarks.

Eddelman is reasonably pertinent to the problem solved by Chan and the instant invention. Both Chan and the instant invention relate to the manipulation and positioning of magnets to introduce foreign matter attached to magnetic microspheres into a population of microorganisms. Eddelman describes how a plurality of magnets may be repositioned along the side of a packing unit to continuously adjust the how magnetic particles interact with a biological solution. Although the end result in Eddelman is different (the separation of an analyte as opposed to the transfection of an

analyte), one of ordinary skill would have found Eddelman's teachings relevant to the positioning of magnetic microspheres of all sizes.

(b) Eddelman uses supports that are sufficiently larger in size and smaller in number. Hence, the present invention cannot be achieved by a simple combination of Eddelman and Chan.

In response, please consider the following remarks.

It is unclear why magnetic particles of varying sizes and number would behave differently when subjected to a similar magnetic pulse. No evidence has been presented on the record as to why the Chan magnets could not be moved in a normal direction before, during and/or after they are activated to begin the introduction of biological material.

(c) The mixture of Dzekunov flows in a single direction, and therefore does not read on the claimed limitation regarding the drawing and discharging of liquid.

In response, please consider the following remarks.

Dzekunov discloses the use of a peristaltic pump (see Figure 12, paragraph [0208] and Table 3 "flow direction") to deliver a biological solution through a test chamber. It is well known in the art that peristaltic pumps are generally multi-directional, and fully capable of drawing and discharging a liquid through and from a passage.

Conclusion

This is a non-final rejection.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NATHAN A. BOWERS whose telephone number is (571)272-8613. The examiner can normally be reached on Monday-Friday 7 AM to 4 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571) 272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nathan A Bowers/
Primary Examiner, Art Unit 1775